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ORIGINAL ARTICLE

Early nutritional intervention improves treatment tolerance and outcomes in head and neck cancer patients undergoing concurrent chemoradiotherapy

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Abstract
Goals of work Patients with head and neck cancer (HNC) undergoing chemoradiotherapy are at high risk of malnutrition, which is related to complication rate. The aim of this study was to investigate the impact of an early intensive nutritional intervention on nutritional status and outcomes in patients undergoing chemoradiotherapy for HNC.
Materials and methods We analysed retrospectively the clinical documentation of 33 HNC patients who were referred for early nutritional intervention (nutrition intervention group, NG) before they were submitted to chemoradiotherapy. The outcome of these patients was compared to that of 33 patients who received chemoradiotherapy without receiving a specifically designed early nutrition support programme (control group, CG).
Main results NG patients lost less weight during chemoradiotherapy compared to CG patients (−4.6±4.1% vs −8.1±4.8% of pre-treatment weight, $p<0.01$, at the completion of treatment). Patients in the NG experienced fewer radiotherapy breaks (>5 days) for toxicity (30.3% vs 63.6%, $p<0.01$); the mean number of days of radiation delayed for toxicity was 4.4±5.2 in NG vs 7.6±6.5 in CG ($p<0.05$); a linear correlation was found between percentage of weight lost from baseline to chemoradiotherapy completion and days of radiation delays ($p<0.01$). There were less patients who had an unplanned hospitalisation in the NG relative to the CG (16.1% vs 41.4%, $p=0.03$). In the NG, symptoms having an effect on the nutritional status developed early and were present in the nearly totality of patients at chemotherapy completion; 60.6% of NG patients needed tube feeding.
Conclusions Early nutrition intervention in patients with HNC receiving chemoradiotherapy resulted in an improved treatment tolerance and fewer admissions to hospital. This result suggests that nutritional intervention must be initiated before chemoradiotherapy, and it needs to be continued after treatment completion.

Keywords Chemoradiotherapy · Enteral nutrition · Head and neck cancer · Nutrition support

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Introduction

Malnutrition is common in patients with head and neck cancer (HNC) [58] and is often characterised by a multifactorial pathogenesis. The anatomic site of the tumour can significantly affect swallowing and chewing functions. Moreover, the majority of these patients have unhealthy feeding habits that predispose to malnutrition, besides having a history of heavy smoking and excessive alcohol consumption [22]. Therapies used for cancer treatment including surgery, radiation and chemotherapy, either alone or in combination, could also negatively influence the nutritional status. At present, concurrent chemoradiotherapy (CRT) seems to be the most appropriate approach in order to preserve organ functions in patients with advanced HNC [12]. However, CRT is often associated with significant acute and late toxicity effects due to its radiosensitisation effects. These may cause severe mucositis preventing oral feeding and often requiring a break in the radiation treatment [20]. The toxic effects can lead to grade 3 or higher mucositis in the majority of patients undergoing CRT, whilst only 20% to 30% of patients treated with conventional radiotherapy (RT) alone will develop mucositis [30]. In a recent review, it has been shown that at 1 month from treatment onset mucositis and dysphagia were developed in 87% of patients treated with CRT [35]. These effects led to an additional 10% of weight loss [39]. The CRT-induced dysphagia, odynophagia, loss of sense of taste, xerostomia, nausea, vomiting and loss of appetite may have a significant negative impact on nutrition and functional ability [6, 21, 34, 46]. Moreover, severe dehydration and malnutrition may lead to unplanned treatment breaks or hospitalisations, thereby compromising treatment efficacy [15]. An overall incidence of 9–19% of RT or radiochemotherapy interruptions due to severe mucositis has been reported [57]. Discontinuation in RT treatment for more than 5 days has been reported in 53% of patients with weight loss >20% during CRT and complete interruption in 29% of these patients [10]. These adverse effects on oral intake abilities may become chronic and may persist even after the tumour has been treated. Approximately 10% of all survivors from HNC will be permanently dependent on enteral nutrition [33]. Although long-term quality of life in patients undergoing CRT is better compared to patients treated with demolitive surgery, it may still be profoundly affected by acute toxicities' effects [8].

Nutrition plays a key role in the care of patients affected by cancer. It is well known that feeding difficulties and weight loss due to the course of the disease and/or its treatment have a significant negative impact in oncology patients [52]. In fact, in cancer patients, malnutrition is associated with longer hospital stays [36], reduced responses to and increased complications from therapies [3, 49], increased costs [49], worse quality of life [42] and lower survival rate [18, 40].

Recent literature has focused on recommendations for early nutrition monitoring and treatment in oncology patients [4, 48]. However, an early nutritional support in HNC patients is not routine at present. Percutaneous endoscopic gastrostomy (PEG) placement before initiation of RT has been shown to prevent weight loss, treatment interruption and hospitalisations [52]. However, PEG has been associated with long-term swallowing disability [2, 35], and currently criteria for patient selection regarding prophylactic PEG placement are not well established.

The aim of our study was to compare the clinical outcomes of two groups of patients affected by HNC, who underwent CRT with different nutritional approach.

Patients and methods

Subjects

Since 2005, in our centre, an early intensive nutritional monitoring and support programme has been specifically created for patients affected by HNC undergoing CRT, within a multidisciplinary management of the disease. Before 2005, patients did not use to be routinely referred to our Dietetic and Nutrition Unit before the beginning of the treatment but only when side effects of the treatment were already present and often occurring late during the therapy's course. Moreover, often patients were not referred until late into treatment.

The clinical documentation of 72 consecutive patients undergoing CRT from 2004 to 2007 was analysed retrospectively. Thirty-nine patients were treated after the implementation of the nutritional programme and were evaluated before the start of CRT. Out of the 39, 33 were compliant to nutritional therapy and follow-up and were designed as nutrition intervention group (NG). Six patients refused the nutritional therapy (oral supplementation or tube feeding) or the scheduled follow-up and were not included in the study. Thirty-three patients were treated before the implementation of the early nutritional programme and were assigned to a control group (CG).

NG patients received nutritional assessment before the beginning of the RT. Ambulatory visits were initially every 7 days throughout the CRT period, followed by 14–28 days of control visits. At the first evaluation, all patients were informed about the potential eating difficulties due to CRT-induced toxicity and about the importance of maintaining a good nutritional status. Patients with stable weight and adequate food intake (low nutritional risk patients) received individualised nutritional counselling by prescription of therapeutic diet with regular foods or texture-modified diets

if dysphagia was present. According to guidelines on nutrition support in adults [56], patients with inadequate food intake for more than 5 days or BMI<18.5 or weight loss>10% in the last 3–6 months or weight loss >5% in the last 3–6 months and BMI<20 kg/m^2 received oral supplements or enteral nutrition (EN) if supplements were not sufficient to maintain an adequate oral intake. Patient's total energy requirements have been estimated using the Harris Benedict equation [24], with an activity factor of between 1.2 and 1.5 and a stress factor of 1.2 applied [5].

EN was usually administered by a nasogastric tube (NGT). PEG was used when EN was indicated early during the CRT (at pre-treatment assessment or in the first week of RT). Oral nutritional commercial supplements were used and consisted of balanced energy-dense, ready-to-use, liquid polymeric formulas (1.5 kcal/mL; 16.7% proteins, 29.5% lipids, 53.8% carbohydrates). A balanced normocaloric or hypercaloric commercial product was used for enteral feeding.

Patients in the CG received the standard practise from the RT centre before 2005, which included general nutrition counselling and a booklet with nutrition advice for RT-induced toxicity. Referral to Dietetic Unit for nutritional intervention usually occurred when symptoms or weight loss were manifest and patients with less severe side effects generally did not receive a specialised evaluation.

Chemoradiation treatment

Patients were prescribed to receive a dose of 66–70 Gy in 33–35 fractions over a period of 7 weeks. All patients received one cycle of neoadjuvant chemotherapy followed by two cycles of chemotherapy concurrently with RT. The chemotherapeutic regimen included *cis*-platinum 100 mg/m^2 on day 1 and 5-fluorouracil 1,000 mg/m^2 as a continuous infusion on days 1–5. The spinal cord was limited to a maximum of 46 Gy. Both sides of the neck were prescribed to receive a boost of electrons with a dose of 4 Gy in patients without neck metastases and 14 Gy in patients with neck metastases. During RT, analgesics, antifungals, vitamin A and mouth rinses were prescribed for all patients. Breaks from radiation treatment were taken in case of severe mucositis (degree≥3), dermatitis (degree≥3) and haematological toxicity following chemotherapy (neutropenia degree≥3; piatrinopenia degree≥3) according to the Radiation Therapy Oncology Group (RTOG) toxicity criteria [51] and National Cancer Institute Common Toxicity Criteria (version 2.0) [38] and in case of weight loss greater than 10% of pre-treatment value or dehydration due to the onset of absolute dysphagia.

The scheduled CRT was the same in NG and in the CG, and the practise of the centre was not different in the two groups as for standards of care and RT delayed procedure.

Data collection

The following data were retrospectively collected from the clinical documentation of both groups at the beginning of CRT (baseline, V0): clinical variables, alcohol abuse and smoking history, cancer site and tumour stage according to TNM classification [54]. Weight changes were evaluated in both groups at the 4th week of RT (V1), at completion of CRT (V2) and at 1 month (V3), 3 months (V4) and 6 months (V5) after the end of CRT.

To evaluate the treatment tolerance, the following data were assessed: number of radiation fractions delayed for toxicity (days), number of unplanned hospitalisations for mucositis and grading of acute RT-induced mucositis, evaluated weekly by the radiotherapist and/or otolaryngologist, with an assigned score from 0 to 4 in accordance with the European Organisation for the Research and Treatment of Cancer/RTOG criteria [51], in which higher scores indicate higher severity.

We further performed a detailed analysis in the NG as for eating ability and dietetic intervention needs, presence of symptoms influencing nutritional status (loss of appetite, vomiting, nausea, dysphagia, xerostomia, taste modifications) and nutritional status, over the treatment period and up to 6 months after the end of CRT. These data were in great measure lacking in the CG documentation to make a comparison. Nutritional intake was derived from a diet history, and changes in food intake were assessed by 24-h recall at each visit. Symptoms influencing nutritional status reported by the patients were assessed by dieticians and recorded in a specifically created case sheet. Nutritional status was assessed by Ottery's Patient-Generated Subjective Global Assessment (PG-SGA) [43], validated for cancer patients: depending on weight changes, symptoms, food intake, functional capacity and physical examination, patients are categorised in three degrees: normal (PG-SGA A), moderate (PG-SGA B) and severe malnutrition (PG-SGA C).

The study was performed according to the ethical standards of the Helsinki Declaration (as revised in 1983).

Statistical analysis

The results were expressed as average±SD. The relation between the single variables was analysed using the chi-squared test for categorical variables. Differences in continuous variables between groups were compared using the Student *t* test for unpaired data. A repeated-measures analysis of variance was used to compare weight changes between groups over time. Correlations were analysed using the nonparametric Spearman test. In order to avoid type 1 error, all *p* values were reported as two-tailed. Statistical analyses were conducted using GraphPad Prism4® software. $P<0.05$ was accepted as statistically significant.

Table 1 Baseline characteristics of nutrition intervention group (NG) and control group (CG)

Characteristics	NG (n=33)	CG (n=33)	p
Age (years)[a]	58.5±10.0	59.0±8.2	ns
Sex ratio (M/F)	24/9	29/4	ns
Weight (kg)[a]	73.5±10.8	72.5±13.2	ns
Body mass index (kg/m^2)*	26.1±3.3	25.3±4.0	ns
Percentage of weight loss in the last 6 months[a]	2.3±4.3	2.7±5.3	ns
Tumour stage II–III/IV (%)	51.5/48.5	39.4/60.6	ns
Smokers (%)	64.3%	75.7%	ns
Alcohol abuse (%)	28%	39.4%	ns
Total dose of planned RT (Gy)[a]	65.3±2.8	66.3±2.2	ns

[a] Data expressed as mean±standard deviation (SD)

ns not significant.

Results

Subjects

Subject characteristics at baseline are detailed in Table 1. No significant differences were found between NG and CG for age, sex, weight, BMI, weight changes in the last 6 months and total dose of RT planned. The rate of stage IV was higher in control group, but the difference did not reach the statistical significance (p=0.25). Also, there were more smokers and alcohol abusers in the CG, but the difference was not found to be statistically significant (p=0.32 and p=0.21, respectively). However, the low sample size may have led to type II error. Table 2 describes the tumour site in the two groups.

Figure 1 shows the mean weight variations (kg) between NG and CG patients over the treatment period and up to 6 months after the end of CRT. Patients in the NG lost significantly less weight than patients in the CG (p=0.024). The percentage of weight loss from baseline in the NG was significantly lower compared to the CG at each evaluation (Table 3). The NG patients underwent major weight loss at the end of treatment (−4.6%) followed by weight regain, whilst patients in the CG continued to lose weight during the 6 months after the end of CRT.

Table 2 Tumour site in nutrition intervention group (NG) and control group (CG)

Tumour location	NG (n=33)	CG (n=33)
Oropharynx	13	20
Hypopharynx	7	7
Nasopharynx	6	3
Larynx	1	3
Oral cavity	3	0
Paranasal sinus	2	0
Parotid	1	0

Effect of nutritional intervention on oncological therapy

Table 4 shows the comparison of treatment tolerance and outcomes in the two groups. No difference was observed in the percentage of patients who completed the planned three cycles of chemotherapy (p=ns). Instead, patients who underwent an RT break for more than 5 days for toxicity were significantly less in the NG (p<0.01). Moreover, the mean number of days of RT delayed because of side effects was significantly lower in the NG than in CG (p<0.05). A significant linear correlation was found between percentage of weight lost from baseline to completion of CRT and the number of days of RT delayed, in all study population (r=−0.35; p<0.01). One patient in the CG refused the last two fractions of radiation and, for one patient in the NG, RT was definitively interrupted at 52-Gy dose for the onset of suppurative parotid infection. No significant difference for grade 3 to 4 mucositis was found between the two groups (p=ns). CG patients had significantly more unplanned hospital admissions during the treatment period compared with the NG (p<0.05).

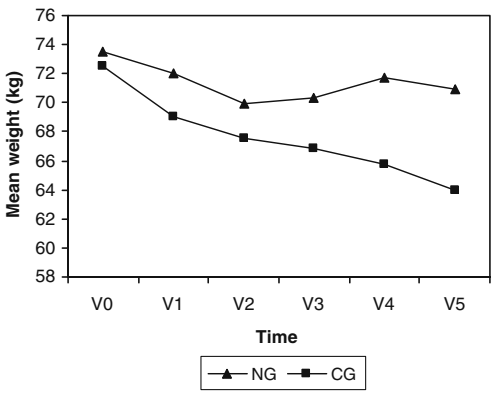

Fig. 1 Mean weight changes in the two groups over CRT treatment period up to 6 months after the end of treatment (p<0.05). (*V0*: pre-CRT, *V1*: 4th week of RT, *V2*: end of CRT, *V3*: 1 months after the end of CRT, *V4*: 3 months after the end of CRT, *V5*: 6 months after the end of CRT)

Table 3 Percentage of weight loss from baseline in the nutrition intervention group (NG). and in the control group (CG)

Time	NG	CG	*p*
V1	−1.72±4.08	−4.70±4.39	0.0057
V2	−4.63±4.08	−8.10±4.82	0.0026
V3	−3.47±5.64	−8.70±3.85	0.0003
V4	−2.77±7.93	−9.75±5.34	0.0009
V5	−2.35±8.15	−9.55±8.10	0.0077

Data expressed as mean±standard deviation (SD)

V1 4th week of RT, *V2* completion of CRT, *V3* 1 month after the end of CRT, *V4* 3 months after the end of CRT, *V5* 6 months after the end of CRT

Eating problems and eating ability in the NG

At pre-treatment evaluation (V0), eight out of the 33 (24.2%) patients in the NG had a weight loss from usual weight (range 3.6–13.3%), two of those had lost more than 5% of usual weight in the last month, whilst the remaining patients (75.8%) had a stable weight (weight loss≤1 kg in the last 6 months). Mean weight loss in the last 6 months was −2.3%.

The frequency of symptoms influencing nutritional status, during the CRT and up to 6 months after completion of treatment, is shown in Table 5. Nausea, vomiting and loss of appetite reached a major frequency ranging between 17.7% and 36.7% at the end of treatment. Swallowing difficulties, taste changes and thick and ropy saliva were present in the majority of patients already at the fourth week of RT and in the nearly totality of patients at the end of CRT. After the treatment, the frequency of these symptoms remained to quite a large extent up to 6 months, and thick and ropy saliva was the most common symptom still present (about half of the patients still had xerostomia at 6 months, one third of patients dysphagia and one fourth of patients taste modifications).

Figure 2 shows the eating ability of patients during the treatment period and up to 6 months. At the fourth week of RT, only two patients (6.1%) had sufficient oral diet; 57.6% were taking oral supplementation and 36.4% needed EN; at the end of CRT, none of the patients had sufficient oral diet and 39.4% had oral supplementation and 60.6% were fed by EN. Mean weight loss in patients treated with oral supplementation was −3.3% of pre-treatment weight, at the end of CRT. Patients with cancer in the nasopharynx, oropharynx or hypopharynx were significantly more often treated with EN than patients with cancer in other sites (p= 0.02). There were no significant differences between patients treated with EN with reference to gender, tumour stage or age (p=ns). None of the patients received parenteral nutrition. Median length of EN was 100 days (range 14–586). Two patients continued EN until they died. Out of the 20 patients who needed EN, 16 were fed by NGT and four were fed by PEG. Out of the 20 who needed EN, 16 (80%) patients were fed exclusively by tube for absolute dysphagia. Mean kilocalories per day infused by tubes in these patients were 2,090±244 in male and 1,833±311 in female. Four patients were fed by tubes maintaining a partial oral nutrition: three females received 1,500 kcal/day and one male received 2,000 kcal/day; mean oral intake in these patients was 460 kcal (range 300–750 kcal). Five patients (15.2%) still needed EN at 6 months (the four patients were fed by PEG and one patient by NGT).

According to PG-SGA, 27.3% of patients were malnourished (PG-SGA B or C) at V0, 75.8% at V1, 84.8% at V2, 64.3% at V3, 39.4% at V4 and 24.3% at V5.

Discussion

Effect of nutritional intervention on outcomes

This study aimed at examining the impact of an early intensive nutritional intervention on nutritional status and clinical outcomes in patients receiving CRT for HNC. Providing intensive nutritional support with regular monitoring reduced the weight loss in patients treated in the NG, compared to the CG, who experienced the typical decrease in body weight. Investigators frequently have reported 10% or greater weight loss of initial body weight during treatment with CRT [9, 29, 39]. This loss cannot be completely prevented by nutritional counselling [14]. However, a randomised study performed in 60 oncology outpatients receiving RT for head and neck or gastrointestinal areas [25] demonstrated that an early, individualised and intensive nutritional intervention resulted beneficial in terms of minimising weight loss, deterioration in nutritional

Table 4 Comparison of treatment tolerance and outcomes for nutrition intervention group (NG) and control group (CG)

	NG (n=33)	CG (n=33)	p value
Patients who completed the planned chemotherapy (%)	96.7	93.9	ns
Grade of mucositis 3–4 (%)	45.5%	39.4%	ns
Patients who had RT breaks (>5 days) for toxicity (%)	30.3	63.6	0.007
Days of RT delayed for toxicity[a]	4.4±5.2	7.6±6.5	0.038
Patients who had a hospital admission for mucositis (%)	16.1	41.4	0.030

[a] Data expressed as mean±standard deviation (SD)

Table 5 Frequency of symptoms influencing nutritional status in NG patients

V0 pre-CRT, *V1* 4th week of RT, *V2* end of CRT, *V3* 1 months after the end of CRT, *V4* 3 months after the end of CRT, *V5* 6 months after the end of CRT

Symptoms	V0	V1	V2	V3	V4	V5
Loss of appetite	9.7%	32.3%	36.7%	25.9%	9.1%	6.1%
Vomiting	0.0%	12.5%	17.7%	14.8%	3.0%	0.0%
Nausea	6.4%	21.9%	28.1%	14.8%	6.1%	3.0%
Swallowing difficulties	10.7%	93.9%	93.9%	80.0%	48.5%	33.3%
Thick and ropy saliva	4.2%	78.6%	96.8%	85.2%	57.6%	51.5%
Taste changes	13.1%	90.0%	100%	76%	42.4%	24.2%

status, global quality of life and physical function. This might suggest that weight maintenance, rather than weight gain, may be a more appropriate aim of nutritional intervention in these patients. Ravasco et al. [47] demonstrated that concurrent individualised dietary counselling, based on regular foods with appropriate manipulation, is the most effective way of improving patients' nutritional intake, status and quality of life, thereby lessening RT-induced morbidity, in HNC patients undergoing RT. However, patients in that study had sequential and not concomitant chemotherapy. Concurrent CRT has demonstrated improved rates of tumour control for locally advanced HNC [17, 19, 44], but it is associated with increased acute toxicity, higher prevalence of weight loss during therapy [7, 14] and more severe oral mucositis [10] compared to RT alone. In our study, we found that the early intensive nutritional support, based on nutritional counselling, oral supplementation and prompt tube feeding, besides a reduction in weight loss, determines a significant improvement in treatment tolerance and reduction in unplanned hospitalisations during CRT. Aggressive nutrition support, involving also the prophylactic placement of PEGs before treatment in patients receiving treatment for HNC and oesophageal malignancies, has shown nutritional status and treatment tolerance benefits accompanied by lower rates of hospitalisation [4, 30, 41, 45, 53]. Capuano et al. [10] observed that a weight reduction greater than 20% of pre-treatment weight significantly increased CRT-induced toxicity and consequent treatment interruptions, infections, early mortality risk and hospital readmission rates within 30 days after CRT completion, whereas early nutritional management reduced weight loss and improved outcome. In our study, a significant difference in outcome was observed even for less severe weight losses. We also found a linear correlation between weight loss and days of radiation treatment delayed for toxicity. This is a critical clinical observation, as treatment interruption due to RT-related toxicity has been reported to be detrimental for loco-regional control and survival in patients with HNC [15, 26, 59]. Therefore, nutritional intervention that facilitates the completion of the planned treatment may give further survival benefits.

The rate of unplanned hospitalisations has important financial and economic implications for the health system. Nutritional support helps in saving the overall health costs by reducing the admissions rate, as the costs of a hospital bed for a day are significantly higher than those for the outpatient management. Moreover, the reduction in hospitalisations may improve the quality of life in these patients [45].

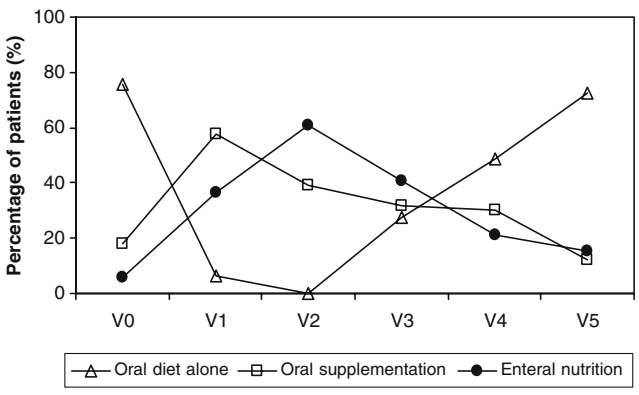

Fig. 2 Eating ability of NG patients during the CRT period and up to 6 months after the end of treatment (*V0*: pre-CRT, *V1*: 4th week of RT, *V2*: end of CRT, *V3*: 1 months after the end of CRT, *V4*: 3 months after the end of CRT, *V5*: 6 months after the end of CRT)

Eating problems and eating ability

Previous studies have shown that patients with HNC often have eating problems and malnutrition when they start RT treatment [11, 32]. Our findings are consistent with these observations and with those showing that eating difficulties during RT are severe and worsen as the dose of radiation increases in time [27, 28, 50, 61]. We found a higher prevalence of eating problems during the treatment than that found by other authors [28] in subjects treated with RT alone. A great number of patients continued to have eating difficulties after the end of the treatment. The most frequent symptoms at 6 months were thick and ropy saliva and taste modifications; difficulties in swallowing were still present in about 30% of patients. Other authors [28] have found that, still at 1 year after completion of RT treatment, the most common eating problem was dry mouth that contributes to reduction in taste and to swallowing difficulties. The persistence of symptoms influencing nutritional status and

risk of malnutrition several months after the completion of treatment reinforces the need for long-term monitoring and support to these patients [13, 23]. In fact, at 6 months after the end of the treatment, 15% of patients still needed EN and 12% oral nutritional supplements for insufficient oral food intake. We did not compare post-treatment side effects and symptoms, for the NG and CG, because these data were not available for the CG.

In our study, patients treated with nutritional intervention received standard diets that were not enriched with immunonutrients. Various nutrients including arginine, glutamine and omega-3 fatty acids have been shown to modulate immune response, and their effects have been studied in cancer patients. Omega-3-enhanced formulas have been suggested to be beneficial in HNC patients during perioperative period [16, 55], but no study has shown significant survival benefit, and further studies are needed to determine the role of immunonutrition in these patients [52].

EN was frequently needed in our patients. The gastrointestinal tract beyond the tumour and treatment site is usually intact; therefore, EN is more appropriate and safer than parenteral nutrition. EN can either be delivered via transanal or percutaneous route. There are no randomised clinical trials comparing PEG with NGT in HNC or oesophageal cancer patients during RT or CRT [4]. Both methods were found to be equally effective at maintaining body weight, but PEG was found to be preferable for greater mobility, better cosmetic appearance and improved subjective quality of life [4, 31], but it may have more complications and morbidity, associated with the placement, being an invasive procedure. Moreover, rare case reports of metastasis of the primary tumour to the gastrostomy site have been documented [1]. Prophylactic placement of PEG, prior to initiation of RT, has been shown to prevent weight loss, treatment interruption and hospitalisation for dehydration [52]. However, PEG has been associated with long-term swallowing disability [2, 35, 37]. In our sample, median EN duration was shorter as compared to the 142 days and 7 months range of EN duration reported in studies conducted in patients treated with prophylactic PEG placement [48]. Currently, criteria for patient selection regarding prophylactic PEG placement are not standardised. In our experience, NGT was safe and well tolerated; we did not observe local or general complications except for accidental removals of the NGT. Moreover, nearly 40% of the patients in our study did not need tube feeding and were able to maintain their weight and good treatment tolerance with intensive dietetic counselling and oral supplementation. In these patients, a prophylactic PEG placement may be disproportionate. Moreover, weight loss experienced by patients in our study is similar or slightly higher to that reported in patients with planned tube feeding ranging between 2.8% and 5% [30, 60], and it is significantly lower than that observed in patients with therapeutic tube insertion ranging about 8.5% and 12% [60]. This suggests a determinant role of the intensive nutritional counselling, in addition to the oral supplementation and the prompt adoption of enteral nutrition in minimising weight loss. However, caring for these patients requires much effort by a nutrition-specialised health staff.

Our study has several limitations: it is not a controlled study, it has a retrospective design and the sample size is relatively small. Moreover, there is no group with prophylactic PEG placement to make a comparison. Moreover, in this study, we do not have data about tumour control and overall survival that is actually of great importance, since no randomised trial has conclusively demonstrated improved survival as result of nutritional intervention during RT. Randomised prospective studies are needed to better define the optimal nutritional management and their impact on survival in patients with HNC undergoing CRT.

In conclusion, intensive nutritional intervention provides beneficial outcomes in terms of reduction of weight loss, interruptions in RT treatment and unplanned hospitalisations in outpatients receiving CRT for HNC. Nutritional intervention must be performed early in order to be successful and long-term follow-up should be provided after completion of CRT.

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Conflict of interest The authors declare no conflict of interest.

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